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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,081	10/03/2003	Hans-Michael Dosch	2560.001	3553
21917	7590	06/08/2005	EXAMINER	
MCHALE & SLAVIN, P.A. 2855 PGA BLVD PALM BEACH GARDENS, FL 33410				LIETO, LOUIS D
		ART UNIT		PAPER NUMBER
				1632

DATE MAILED: 06/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/679,081	DOSCH ET AL.
	Examiner	Art Unit
	Louis D. Lieto	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 25 April 2005.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 2 and 5 is/are pending in the application.
 - 4a) Of the above claim(s) 1,3 and 4 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 2 and 5 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 03 October 2003 is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>6/14/2004</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's response to the Restriction was received on 4/25/2005. Claims 1-15 are pending in the instant application. Applicant's election without traverse of group II, drawn to claims 2 and 5 in the reply filed on 4/25/2005 is acknowledged.

Claims 1, 3 and 4 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/25/2005.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Information Disclosure Statement

The information disclosure statement filed 6/14/2004 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. Applicant only provided the abstracts for several of the references listed. Therefore, the examiner only considered the abstracts of these references.

Drawings

The drawings are objected to under 37 CFR 1.83(a) because they fail to show the histological details and banding patterns as described in the specification. Specifically, the

Figures 1-3 contain subsections which are not listed in the Brief Description of the Figures.

Applicant is required to amend the Brief Description of the drawings in the Specification to describe each component of the figures (e.g. A,B,C, etc.), or to provide corrected drawings removing the undescribed material. Corrected drawing sheets are required in reply to the Office action to avoid abandonment of the application. Any amended replacement-drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as “amended.” If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled “Replacement Sheet” in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the examiner does not accept the changes, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 2 and 5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The claims are drawn to any high affinity mimicry peptide targeting ICA69- specific T cells from any species. The claims encompass a genus of mimicry peptides defined solely by the fact that they have a high affinity for ICA69-specific T cells.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. The only member of the genus contemplated in the specification is the ABBOS peptide (Specification pg.5, lines 9-22).

The factors to be considered when assessing possession of the claimed invention include disclosure of complete or partial structure, physical and/ or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In the instant case, the only factor present in the claims is the requirement that the mimicry peptides have a high affinity for ICA69-specific T cells.

The specification does not contemplate any sequence that these peptide must share or the structure of any epitopes they must mimic in order to bind to ICA69-specific T cells. Further, Karges et al. teaches that antigen mimicry and its structural perquisites are not well understood, and that strong linear homology between two peptides is not predictive of successful mimicry responses{Karges et al. (1997) Diabetes 46 :1548-1556; pg. 1554, col. 1, pgph 3}. Accordingly, in the absence of sufficient recitation of a distinguishing identifying characteristic, the

specification does not provide adequate written description of the a genus of mimicry peptides defined solely by the fact that they have a high affinity for ICA69-specific T cells.

The Revised Interim Guidelines state, "when there is substantial variation with the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (Column 2, page 71436, or the Revised Interim Guidelines for Written Description). Case law concurs, stating, "simply describing large genus of compounds is not sufficient to satisfy written description requirement as to particular species or sub-genus" *Fujikawa v. Wattanasin*, 39 USPQ2d 1895 (CA FC 1996). Furthermore, *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). Thus, the specification does not meet the written description provision of 35 U.S.C. 112, first paragraph, for any genus of mimicry peptides defined solely by the fact that they have a high affinity for ICA69-specific T cells. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision.

Claims 2 and 5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an immunotherapeutic process for treating a NOD mouse

suffering from primary Sjogren's Syndrome with an ABBOS high affinity mimicry peptide targeting ICA69-specific T cells in a manner effective to induce tolerance to a ICA69, whereby the symptoms characteristic of primary Sjogren's syndrome are treated, such as a reversal of sialoadenitis and dacryladenitis , does not reasonably provide enablement for an immunotherapeutic process for treating any individual suffering from primary Sjogren's Syndrome with any high affinity mimicry peptide targeting ICA69-specific T cells in a manner effective to induce tolerance to a relevant ICA69 epitope, whereby the symptoms characteristic of primary Sjogren's syndrome are treated, such as a reversal of sialoadenitis and dacryladenitis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims encompass treating any individual from any species that suffers primary Sjogrens Syndrome (pSS), with any high affinity mimicry peptide targeting ICA69-specific T cells, which reduces the symptoms characteristic of primary pSS, where the symptoms may be sialoadenitis and dacryladenitis.

The specification does not provide an enabling disclosure for using any high affinity mimicry peptide, other than the ABBOS peptide, in any species other than a NOD mouse. The only working examples disclosed that provide enablement for treating pSS, were performed in NOD mice using the ABBOS peptide. The specification does not describe any methods of constructing other mimicry peptides or even what aspects of the Tep69 self-epitope must be mimicked by other peptides in order to induce tolerance rather than increased auto immunity. Further, Karges et al. teaches that antigen mimicry and its structural perquisites are not well understood, and that strong linear homology between two peptides is not predictive of successful

mimicry responses{Karges et al. (1997) Diabetes 46 :1548-1556; pg. 1554, col. 1, pgph 3}. The mouse ICA69 protein is 483 amino acids long {Pietropaolo et al. (1993) J. Clin. Invest. 92:359-371}. The specification does not provide any evidence that any other epitope other than Tep69 is associated with pSS or that a peptide mimicking any other ICA69 epitope can induce T-cell tolerization and treat pSS. Finally, the specification does not provide any guidance that ICA69, and especially the Tep69 epitope, has significant sequence or structural homology between mice and any other species known to acquire pSS.

Finally, as the inventors note in their 2002 publication describing their work:

Because of the diversity and variability of human Sjögren's syndrome, translation of data from the NOD mouse to human disease must be met with caution....We have previously associated the efficiency of ABBOS immunotherapy in diabetes prevention with its high affinity binding to MHC, where tolerance of ABBOS was dose-dependent, and disease was exacerbated at suboptimal doses. This association raises caution in the translation of mouse to human data, especially with the choice of peptide and peptide doses.

Winer et al. (2002) The Lancet. 360 :1063-1069 ; pg.1068, col.1-2 bridging pgph

These statements indicate that the inventors doubt that results observed in their mouse model using the ABBOS peptide to induce tolerance can be used to predict the efficacy of using such a treatment with the ABOSS peptide in humans for a method of immunotherapy to treat pSS. Further, the specification does not disclose any mode of administration for treating pSS in any individual, such as the amount of high affinity mimicry peptide to be administered, the number of times it is to be administered, the duration of time involved and the route of administration. The specification does not disclose that administering the peptide by any route, such as orally or via a transdermal patch can treat pSS. The specification lacks enablement, absent a disclosure indicating that the NOD mouse model described, or any NOD mouse model,

can be used to reliably predict that a peptide used to treat an autoimmune disease in the NOD model can also be used to treat the same disease in humans.

Given the lack of guidance in the specification on the use of any mimicry peptide to treat pSS in any species, the lack of working examples disclosing such a treatment in any species other than mice, the lack of disclosure on the conditions of administration of any mimicry peptide in any species in order to treat pSS, the teachings in the art that basing a treatment of pSS in humans on the results observed in mice is unpredictable, and the lack of teachings in the specification on any other self-reactive ICA69 epitope other than Tep69, the skilled artisan would be unable to predict how to practice the invention as claimed, except as an immunotherapeutic process for treating a NOD mouse suffering from primary Sjogren's Syndrome with an ABBOS high affinity mimicry peptide targeting ICA69-specific T cells in a manner effective to induce tolerance to a ICA69, whereby the symptoms characteristic of primary Sjogren's syndrome are reduced, such as a reversal of sialoadenitis and dacryadenitis, without undue and extensive experimentation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

- (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 2 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Karges et al. {Karges et al. (1997) Diabetes 46 :1548-1556}, further in view of Humphreys-Behr {Humphreys-Behr (1996) Adv. Dent. Res. 10:73-75}.

Karges et al. provides guidance on treatment of NOD mice with the ABBOS mimicry high-affinity peptide, in order to induce T-cell tolerance to ICA69 (Abstract). Further Karges et al. teaches that administration of the ABBOS mimicry peptide reduced diabetes incidence in NOD mice (pg. 1554, col.1, pgph 1554) and was able to induce cross-tolerance to the Tep69 epitope of ICA69 autoantigen (pg. 1551, Fig. 3). Karges does not treat these NOD diabetic mice have pSS.

Humphreys-Behr supplements the guidance of Karges et al. by teaching that the diabetic NOD mouse model also undergoes a corresponding loss in exocrine gland function related to lymphocyte infiltrates symptomatic of the pathophysiology of primary Sjogrens Syndrome.

Based on the guidance provided by Karges et al. on a method of treating an diabetes in NOD mice with the ABBOS mimicry high-affinity peptide by inducing tolerance of the mouse's ICA69 specific T-cells to ICA69, and the guidance of Humphreys-Behr that some diabetic NOD mice develop pSS, it would be *prima facie* obvious to the person of ordinary skill in the art at the time the invention that treatment of diabetic NOD mice with the ABBOS mimicry high-affinity peptide that induced tolerance in ICA69 specific T cells to ICA69 would also treat any other disease caused by the activity of ICA69 specific T cells, such as pSS in the same mouse.

A practitioner in the art would be motivated to treat NOD mice with diabetes and pSS with the ABBOS peptide in order to induce tolerance of the mouse's ICA69 specific T-cells to ICA69 and thus to treat the diabetes.

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The person of ordinary skill in the art would have a reasonable expectation of success because the method of Karges et al. treats diabetes in the mouse by inducing tolerance in ICA69 specific T cells and therefore any other diseases caused by these ICA69 specific T cells would also be treated by the induction of tolerance.

No claims allowed.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Lou Lieto whose telephone number is (571) 272-2932. The examiner can normally be reached on Monday-Friday, 9am-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571)-272-0735. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Patent applicants with problems or questions regarding electronic images that can be viewed in the PAIR can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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